Reference is made to the following documents:

D1: US 2003/212092

D2: WERMUTH ET AL: "The Practise of Medicinal Chemistry" PRACTICE OF

MEDICINAL CHEMISTRY, 1996, pages 203-237

## Re Item III

Claims 14-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

## Re Item V

1) The subject-matter of present claims 1-18 is new (Article 33(2) PCT).

The document D1 discloses immunomodulators of formula (I) (cf. claim 1 and examples 2, 3, 7-10, 23, 108, 115, 116, 118, 120, 122, 123, 146, 147 and 149).

The subject-matter of the present claims 1, 2, 17 and 18 differs from the compounds of D1 in that the substituent on the ring nitrogen atom does not comprise an oxygen atom in the linker X'-Z. Therefore, the claims are novel.

The dependent claims and the claims relating to the use of the new compounds are novel by consequence (Claims 3-12 and 14-16).

The claim 13, relating to a composition comprising the novel compounds, is also novel.

 The subject-matter of claims 1-18 does not involve an inventive step (Article 33(3) PCT).

The document D1 represents the closes prior art (cf. above).

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

PCT/US2004/042556

The technical problem underlying the present claims 1 and 2 is seen in the provision of alternative immunomodulators.

The problem appears to be solved by the replacement of the oxygen atom in the residue X-O- $R_1$  of D1 by a  $CH_2$  group (cf. claim 1 and examples 2, 3, 7-10, 23, 108, 115, 116, 118, 120, 122, 123, 146, 147 and 149 of D1).

However, such an isosteric replacement does not involve an inventive step when the modified compounds only exhibit the same activity as the current compounds (see D2, page 209).

The present claims would only involve an inventive step if the claimed compounds showed unexpected properties or effects compared to the above mentioned compounds of D1.

The claims relating to a pharmaceutical composition, the claims relating to the use of the compounds and the claims relating to synthetic precursors of the compounds according to claim 1 and 2 would only involve an inventive step if the claims 1 and 2 fulfilled this requirement.

## Remark

The term "non-interfering substituent" used in claim 1 does not satisfy the requirements of Article 6 PCT.

The term is to be seen as a functional feature. Functional features are, however, allowable only if the result is one which can be directly and positively verified by tests or procedures adequately specified in the description or known to a person skilled in the art and which do not require undue experimentation (cf. Guidelines, II, 5.35).